REMARKS

Status of the Claims

Claims 1, 2, 8, 10-33 and 56 were presented for examination and were rejected. Claims 3-4 and 34-55 were withdrawn by the Examiner as being drawn to non-elected inventions. In this amendment, claims 10-12 are canceled without prejudice or disclaimer, and claim 1 is amended to clarify the invention. Support for the amendment is found, for example, in original claim 12 and at page 5, lines 13-21; page 19, lines 13-14; and page 22, line 24 – page 23, line 2 of the application as filed. No new matter has been added. Upon entry of this amendment, claims 1, 2, 8, 13-33 and 56 will be pending a subject to further examination. Entry of the amendment and reconsideration on the merits in view of the following comments is respectfully requested.

With respect to all amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Rejection under 35 U.S.C. § 103

Claims 1, 2, 8, 10-33 and 56 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Fletcher *et al.* (*J. Gen. Microbiol.* 1976, 94:400-404, "Fletcher") in view of Kemshead & Ugelstad (*Mol. Cell. Biochem.* 1985, 67:11-18, "Kemshead") and Rudi *et al.* (*Appl. Environ. Microbiol.* 1998, 64:34-37, "Rudi").

The Office has asserted that Fletcher teaches a method of recovery of marine bacteria from environmental samples using the well-known property inherent in polystyrene to non-specifically affix proteins and cells to the surface. Fletcher is cited solely to establish that it has long been known that untreated polystyrene *per se* is useful for non-specific biological sample concentration

resulting in viable organisms. The Office has acknowledged that Fletcher does not teach magnetic microbeads or any of the additional limitations of claims 2, 8, 10-33 and 56.

The Office has further asserted that Kemshead teaches the use of magnetic materials for medical applications. The Office has alleged that Kemshead teaches separation methods using magnetic microbeads for a variety of cell types, using both non-specific binding and specific binding partners. Thus, the Office has concluded that the combination of Fletcher and Kemshead teaches that many types of cells can be separated and enriched from dilute environmental and clinical samples using magnetic polystyrene beads under a wide variety of conditions. Finally, Rudi allegedly teaches a method of using magnetic microbeads to sequentially separate bacteria from environmental samples and amplify separated DNA using the same magnetic microbeads.

The Office has asserted that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Fletcher by substituting unmodified magnetic microbeads for polystyrene Petri dishes as taught by Kemshead and/or Rudi. The skilled artisan allegedly would have been motivated to do so because of the nonspecific adhesion of cells to polystyrene as taught by Fletcher and the rapidity of magnetic bead separation as taught by Kemshead and/or Rudi. The Office further has alleged that there would have been a reasonable expectation of success, given well-known absorptive properties of polystyrene, as taught by Fletcher and the general utility of magnetic bead separation methods as taught by many researchers especially including Kemshead and/or Rudi.

The rejection is moot with respect to claims 10-12 because these claims are canceled. With regard to claims 1, 2, 8, 13-33 and 56, Applicants respectfully traverse this rejection.

As an initial matter, claim 1 has been amended to recite additional limitation "the magnetic microbead has a diameter of 200 nm and is modified to comprise a hydroxyl, a carboxyl or an epoxy group." As noted above, this amendment is supported by the original claim 12 and by the following passages in the specification as filed:

> [T]he magnetic micro-beads modified with hydroxyl, carboxyl and epoxy groups have better separation effect. It is not necessary to treat the magnetic micro-beads with other chemical treatment methods.
>
> (WO 2004/053115 Al at page 19, lines 13-15, emphasis added.)

> It is shown that the magnetic micro-beads with the diameter of 200 nm have the best separation effect, with 75% separation efficiency at pH 5.5. Using the magnetic micro-beads among the diameters from 20 to 100 nm, there is little difference in the separation efficiency, which is about 50%. The separation efficiency is about 30% using the micro-beads with the diameter of above 300 nm. After modification, the separation efficiency of the magnetic micro-beads increases 15-30%.
>
> (WO 2004/053115 Al at page 22, line 24 – page 23, line 2, emphasis added.)

Thus, the present application discloses that relatively minor changes in the size of the magnetic beads had an unexpectedly strong effect on the leukocyte separation efficiency. The optimal separation efficiency was obtained when 200 nm magnetic beads were used, with marked decreases in separation efficiency observed at less than 100 nm and more than 300 nm bead diameters. Importantly, when the surface of 200 nm magnetic beads was modified with a hydroxyl, carboxyl or epoxy groups, the leukocyte separation efficiency approached 90-100%, which had not been previously reported in the absence of a specific binding agent (e.g., an antibody).

Although some prior art references appear to suggest generally that nonspecific binding could be used to isolate a target cell from a sample, it is respectfully submitted that none of the cited prior art references, alone or in combination, specifically discloses all the limitations of claim 1 as amended. Moreover, there is nothing in the prior art that would teach or suggest that a high rate of separation, such as the one disclosed in Example 1, could be achieved in approximately 15 minutes at room temperature without using antibody-modified magnetic beads.

Because the cited prior art references fail to teach or even suggest each and every limitation of the claimed invention, Applicants respectfully submit that this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 514572000600. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: June 29, 2009

Respectfully submitted,

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